REMARKS

Reconsideration and withdrawal of the rejections set forth in the Office Action dated March 14, 2008 are respectfully requested in view of the foregoing amendments and following remarks.

I. Amendments to the Claims

Claim 24 is amended to recite, "produced as an intermediate compound by treating 5-cyanophthalide with a mixture of 4-fluorophenyl magnesium halide and 3-dimethylaminopropyl magnesium halide." Support for the added language can be found, e.g., page 3, lines 8-14, of the specification.

No new matter has been added by these amendments.

II. Rejection under 35 U.S.C. § 112, first paragraph

Claims 24 and 26 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly unsupported by an enabling disclosure with respect to the claimed compound. In particular, the Examiner states that, "even if the indicated structure is initially formed, it would eventually form the other possible magnesium alkaloid" and that "such organometalic alkoxides form aggregates and not discrete structures" (Office Action at 2).

The rejection is respectfully traversed.

A. Analysis

The test of enablement is whether one reasonably skilled in the art could make or use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation. A patent may be enabling even though some experimentation is necessary. *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217 (Fed. Cir. 1988).

Claim 24 recites a compound of the indicated structure that is "produced as an intermediate compound by treating 5-cyanophthalide with a mixture of 4-fluorophenyl magnesium halide and 3-dimethylaminopropyl magnesium halide." The added claim

language makes clear that the indicated structure is an intermediate formed by a particular reaction, as described in the specification at, e.g., page 3, lines 8-14.

The Examiner asserted that "the indicated structure . . . would eventually form the other possible magnesium alkaloid." (Id.) However, even if, *arguendo*, the indicated structure eventually forms "the other possible magnesium alkoxide," one skilled in the art can still make and use the claimed intermediate compound by following the guidance provided in the specification. For example, a skilled artisan can make the claimed compound following the claimed steps and the teaching the specification, and can use the compound for preparing citalopram according to methods known in the art. For these reasons, Applicants submit that the the specification is enabling for the full scope of the claimed compound.

The Examiner also asserted that organometallic compounds are known to aggregate rather than form discrete compounds. Applicants submit that there is no evidence of record to suggest that the particular claimed magnesium alkoxide intermediate compound aggregates and could not be found in discrete form. A cursory review of the literature suggests that while aggregation of some organometallic compounds is known to occur, solvents such as tetrahydrofuran (THF) can be used to solubilize such aggregates.[1] Note that THF was used in the present reactions (e.g., bottom of page 5). Moreover, the fact that Applicants were able to obtain NMR data from a preparation of the intermediate compound demonstrates that at least some discrete compounds were necessarily present in the sample. Thus, the specification adequately demonstrates the presence of the claimed intermediate and fully enables one skilled in the art to make and use the claimed intermediate without undue experimentation.

In the event that any portion of the enablement rejection is maintained in a future Office Action, Applicants request that Examiner clearly articulate what undue experimentation would be required to make or use the claimed invention.

Withdrawal of the rejection is respectfully requested.

[1] Applicants will provided such references as need to rebut a properly supported rejection if issued in a future Office Action.

III. Rejections under 35 U.S.C. § 103

Claims 1-10 and 15-25 were rejected as allegedly obvious under 35 U.S.C. § 103 over EP 017943 (Bogeso).

Claims 1 and 12-25 were rejected as allegedly obvious under 35 U.S.C. § 103 over U.S. Patent No. 4,943,590 (Bogeso).

These rejections are respectfully traversed.

A. The Pending Claims

The claimed method, as exemplified by claim 1, relates to a "process for the preparation of citalopram, comprising (a) treating 5-cyanophthalide with a mixture of 4-fluorophenyl magnesium halide and 3-dimethylaminopropyl magnesium halide and, without isolating an intermediate, (b) adding an organic acid, an inorganic acid, or triphenylphosphine and ethyl azadicarboxylate, thereby producing citalopram without isolating an intermediate.

B. The Cited Art

EP 0171943 and USPN 4,943,590 describe methods for performing the dehydration of a diol, both methods requiring discrete reaction steps for forming an intermediate and then affecting cyclization on the isolated intermediate. As described in the *Background* section of the present specification, the reaction between 5-cyanophthalide and 4-fluorophenyl magnesium bromide to produce intermediate (A), and the reaction between intermediate A and 3-dimethylaminopropyl magnesium chloride to produce a first magnesium intermediate (B), are both very slow, requiring an overnight incubation.

C. Analysis

The basis for the maintained rejections appears to be that "Applicant has not shown any unexpected results in the instant process" (Final Office Action dated March 14, 2008, page 4). In response, Applicants respectfully note the following.

As discussed in the *Background* section of the specification as filed, the cited Bogeso references, EP 0171943 and USPN 4,943,590, require an *overnight*

incubation to produce the first magnesium intermediate, which is a slow, multi-step reaction. Bogeso's need for an *overnight* incubation is illustrated, e.g., in example 1 of EP 0171943.

In contrast, the claimed process is fast, and upon addition of the two Grignard reactants to the 5-cyanophthalide the reaction is essentially complete, providing the product of claim step (a) immediately available for step (b) of the process. Elimination of an overnight incubation step, and/or speeding a chemical reaction step, represents a clear and unexpected advantage in the chemical synthesis of citalopram, which is nowhere taught or suggested by any reference of record, separately or in combination. Since the present claims recite a process that is neither taught nor suggested by the prior art references and provides clear unexpected advantages over existing methods, Applicants submit that the claims patentably define over the prior art.

Applicants note that claim 27, added in the previous Response, was not identified in the present obviousness rejection. To the extent the rejection was intended to apply to claim 27, the remarks above apply equally.

In view of the foregoing, Applicants respectfully request withdrawal of the rejection is respectfully requested.

IV. Conclusion

In view of the foregoing, Applicant submit that the claims are fully in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If the Examiner has any questions or believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (650) 838-4441.

Respectfully submitted,

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